Assessment of pericardial constraint in dogs

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ABSTRACT To determine the better method of measuring pericardial constraint, pericardial pressure was recorded by a liquid-filled open-ended catheter and a liquid-containing flat balloon in six open-chest anesthetized dogs. Left ventricular pressure was measured by a micromanometer-tipped catheter and left ventricular anteroposterior diameter was measured by sonomicrometry. Left ventricular end-diastolic pressure was raised to 20 ± 1.7 (mean ± SD) mm Hg by intravenous saline. Left ventricular diastolic pressure-diameter loops were constructed (1) with incremental amounts of saline (0 to 50 ml) in the resealed pericardium, (2) with several small holes in the pericardium, and (3) with the pericardium widely open. Measured pericardial pressures were compared with what was assumed to be the correct pericardial pressure, i.e., the calculated difference between left ventricular diastolic pressure (at a given left ventricular diameter) before and after opening the pericardium. Pressure recorded by the flat balloon was similar to the calculated pericardial pressure at all pericardial liquid volumes. Pressure recorded by the open-ended catheter, however, was significantly lower (p < .05) than the calculated pressure unless there was at least 30 ml of liquid in the pericardium. After several holes had been made in the pericardium it still exerted a constraining effect, as shown by a marked rightward or downward shift of the left ventricular diastolic pressure-diameter relationships after completely opening the pericardium. After holes were made in the pericardium pressure recorded by the flat balloon was still similar to the calculated pericardial pressure. However, pressure recorded by the open-ended catheter was significantly (p < .02) lower than the calculated pressure. In four dogs the product of left ventricular anteroposterior and septum-to-free wall diameter was used as a volume parameter; comparison made between measured and calculated pericardial pressures confirmed the results obtained with use of anteroposterior diameter to assess left ventricular size. In conclusion, unless the pericardium is sealed and contains at least 30 ml of liquid, an open-ended catheter significantly underestimates pericardial constraint. However, a flat liquid-containing balloon correctly measures pericardial constraint regardless of the amount of pericardial liquid and also when the pericardium is not sealed. Circulation 71, No. 1, 158–164, 1985.

THE QUANTITATIVE EFFECT of pericardial constraint on left ventricular diastolic function remains controversial.1–3 It seems clear that the resolution of this controversy depends on the magnitude of pericardial pressure that, in turn, depends on the method of measurement. In the pulmonary literature Agostoni and others4–6 have promulgated the distinction between “liquid pressure” and “surface pressure.” Liquid pressure is familiar to cardiovascular physiologists and can be measured by connecting a manometer to any fluid-filled space as with a liquid-filled catheter. The concept of surface pressure is more difficult; it is the force per unit surface area exerted by, for example, the left ventricular surface on the overlying parietal pericardial membrane. The difference between the pericardial liquid pressure and surface pressure is the compressive contact stress7 developed between the surfaces.4

The oft-quoted work by Kenner and Wood1 supports the common view that pericardial pressure is approximately equal to intrathoracic pressure and unchanged by alterations in cardiac volume. They dilated the heart substantially by aortic and pulmonary artery constriction without importantly raising pericardial (liquid) pressure. Some years ago Holt et al.2 used a liquid-containing balloon and demonstrated that blood volume expansion increased pericardial (surface) pressure.
nearly as much as it increased left ventricular diastolic pressure. Recently, using a similar balloon, we have demonstrated important changes in pericardial (surface) pressure following changes in preload or afterload in the failing heart.8

Thus, the aim of the present study was to determine whether an open-ended catheter or a flat, liquid-containing balloon could accurately measure pericardial constraint. To arrive at a “gold standard” of pericardial pressure we postulated a simple, static-equilibrium concept: at a given left ventricular end-diastolic size (diameter) the correct pericardial pressure is that pressure which must be added to left ventricular transmural pressure to equal the intracavitary left ventricular pressure. We measured left ventricular transmural pressure directly as a function of left ventricular diameter at the end of the experiment after removal of the pericardium with the chest widely open and the lungs retracted. Thus, we defined the calculated pericardial pressure as the difference between the left ventricular end-diastolic pressure measured when the pericardium was closed and the left ventricular end-diastolic pressure measured at the same diameter when the pericardium was removed. To determine the dependence of the measured pericardial pressure on the volume of pericardial liquid we infused saline into the resealed pericardial cavity. To test the hypothesis that even a netlike pericardium would induce a measurable, physiologically significant constraint on left ventricular diastolic filling, measurements were repeated after several small holes had been cut in the pericardium.

Methods

Animal preparation. Experiments were done in six mongrel dogs (22 to 33 kg). Anesthesia was induced by 25 mg/kg iv sodium thiopental (Pentothal, Abbott Laboratories, Montreal, P.Q.) and was maintained by 1.5% halothane and nitrous oxide/ oxygen with use of a constant-volume respirator (model 607, Harvard Apparatus Co. Inc., Millis, MA) and a closed rebreathing system. A midline sternotomy was performed with each dog in the supine position. Left ventricular pressure was measured by a No. 8F micromanometer-tipped catheter with a reference lumen (model PC-480, Millar Instruments, Houston, TX). The ventral surface of the pericardium was incised transversely along the base of the heart. A flat balloon and open-ended catheter were positioned on the anterolateral surface of the left ventricle at the mid left ventricular level and were stitched loosely to the epicardium. The open-ended catheter was composed of a 4 cm terminal silicone rubber segment with an end-hole and three side-holes fixed to a stiff 60 cm No. 8F cardiac catheter. Another multiple side-hole catheter was inserted into the pericardium to be used for drainage and saline infusion. The pericardium was sutured and sealed water tight by applying small amounts of glue (The Gripper Super Glue, Via Chem., Inc., Quebec, P.Q.) along the sutures. A snare was placed around the posterior vena cava to transiently restrict left ventricular filling and a catheter for intravenous infusion was placed in a femoral vein. Aortic pressure was monitored through a catheter introduced into a femoral artery. Left ventricular anteroposterior diameter (DAp) and in four dogs septum-to-left ventricular free wall diameter (DSFW) were measured with ultrasonic crystals. The free wall crystals were sutured to the epicardium at the mid left ventricular level. The septal crystal was pushed halfway through the septum at the mid left ventricular level. A limb-lead electrocardiogram was monitored and body temperature was maintained by a warming lamp.

Pressures, diameters, and the electrocardiogram were recorded (Electronics for Medicine/Honeywell, model VR16, White Plains, NY) at a paper speed of 75 mm/sec. Data were also recorded on analog tape (Hewlett Packard, model 3966A, Palo Alto, CA) for later analysis.

Pericardial balloons. The balloons were made from a 0.025 cm thick folded sheet of silicone rubber (Armet Industries Corp., Concord, Ont.) sealed at the edges. (Internally, the balloon measured 3 x 3 cm.) A short silicone rubber tube protruding from the balloon was connected to a 60 cm No. 8F stiff cardiac catheter. The balloon could hold up to 1.8 ml of fluid without developing measurable pressure. Before insertion into the pericardium, the balloon was calibrated by a procedure similar to that used by McMahon et al.,9 the results of which are illustrated in figure 1. The balloon was also found to accurately measure negative pressures (0 to −20 mm Hg) that were created in a water-containing chamber.

The frequency response of the balloon was tested in a water chamber (WGA-200, Millar Instruments, Inc., Houston, TX). The pressure amplitude ratio (balloon-micromanometer) was 1.0 below 14 Hz and increased to 1.1 at 25 Hz (both amplifiers filtered at 2500 Hz).

Experimental protocol. To increase pericardial pressure, the dogs received intravenous infusions of saline adjusted to maintain left ventricular end-diastolic pressure at approximately 20 mm Hg (mean ± SD = 20.2 ± 1.7 mm Hg) throughout the period of pericardial saline infusion. Pericardial suction was applied initially and was discontinued immediately before the first (pericardium empty) recording. Then saline was infused into the pericardium at a rate of 7.6 ml/min with use of an infusion pump (model 940, Harvard Apparatus Co., Inc., Millis, MA) and pressure and diameter recordings were taken with 5, 10, 20, 30, 40, and 50 ml of fluid in the pericardium.

To determine whether the pericardium restricted left ventricular diastolic filling even after it had been perforated, recordings were made in five dogs after four or five 5 mm slits had been made in the ventral and lateral surfaces of the pericardium.

Finally, recordings were made with the pericardium widely opened. Left ventricular diameters comparable to those recorded earlier in the experiment were obtained by moderate bleeding and by reducing flow in the posterior vena cava.

Data analysis. To arrive at a gold standard of pericardial pressure we assumed that at the endocardial surface at end-diastole left ventricular pressure was balanced by the sum of left ventricular transmural pressure (PLVTm) and pericardial pressure (PP) as follows: PLVTm = PLVT + PP and, therefore, PP = PLVT − PLVTm at any given left ventricular diameter.

Left ventricular pressure vs DAp loops were constructed by an analog computer (MiniAc, Electronics Associates, Inc., West Long Branch, NJ). The diastolic portions of a series of pressure-diameter loops recorded when the pericardium was widely opened were assumed to represent the directly measured left ventricular transmural pressure-diameter relationship. The vertical difference between the left ventricular transmural pressure-diameter loop and the left ventricular transmural pressure-diameter loop was defined as the calculated pericardial pressure (Pcal) (figure 2). At end-diastole (defined as the end of the A wave), this value was compared with pressure measured by the pericardial open-ended catheter (PP,) and balloon (PPb).
We calculated pressures of differences between pericardial and the balloon. The addition of the volume-squared term had no significant effect on the amount of unexplained variance and a linear fit was used. The values for measured pericardial pressures as percentages of PP_{calc} were compared by two-way analysis of variance with data groups consisting of PP_{calc}, PP_{b}, and PP_{a}, respectively (H_{0}; pressure differences = 0). When the F ratio indicated a difference we used Student’s t test for unpaired observations to determine the level of significance. A probability value of less than .05 was considered to indicate significance.

Results

Figure 3 shows left ventricular pressure-diameter loops from a representative experiment. Note that when the pericardium is empty or contains small amounts of fluid, the left ventricular transmural pressure calculated by subtracting pericardial pressure measured by open-ended catheter exceeds the directly measured transmural left ventricular pressure. Table 1 and figures 4A and 4B show how much the measured pericardial pressures deviate from PP_{calc} (compared at end-diastole). When the pericardium was empty, the open-ended catheter measured a pressure that averaged 12.6 mm Hg less than the calculated pressure. With progressive infusion of fluid into the pericardium, the

![Picture of a quadratic curve](P = a + bV + cV^2). For the catheter the introduction of the volume-squared term significantly (p < .005) reduced the amount of unexplained variance and the quadratic curve was therefore used. For the balloon the addition of the volume-squared term had no significant effect on the amount of unexplained variance and a linear fit was used. The values for measured pericardial pressures as percentages of PP_{calc} were analyzed in the same fashion. For each curve 95% confidence limits were calculated (H_{0}; pressure differences = 0). In the five dogs in which we made incisions in the pericardium and in the four dogs in which the product of D_{A,p} and D_{S,FW} diameters were used to assess left ventricular volume, measured pericardial pressures and PP_{calc} were compared by two-way analysis of variance with data groups consisting of PP_{calc}, PP_{b}, and PP_{a}, respectively (H_{0}; pressure differences = 0). When the F ratio indicated a difference we used Student’s t test for unpaired observations to determine the level of significance. A probability value of less than .05 was considered to indicate significance.
FIGURE 3. Pressure-diameter loops from a representative experiment. In each panel the amount of pericardial fluid is indicated on the top. There is a single loop representing left ventricular pressure ($P_{LV}$) with the pericardium closed (----), and single loops representing $P_{LV}$ minus $P_{c}$ (-----) and $P_{b}$ (---------), respectively. $P_{LV}$ with pericardium open (-----) is indicated by three separate loops; these loops represent the directly measured transmural $P_{LV}$. Note that transmural $P_{LV}$ calculated by subtracting pressure in the flat balloon approximates the directly measured transmural $P_{LV}$. Transmural $P_{LV}$ calculated by subtracting $P_{c}$ however, is higher than the directly measured transmural $P_{LV}$ unless there is at least 30 ml of fluid in the pericardium.

The pressure measured by the open-ended catheter came closer to the calculated pressure (figures 4A and 4B). The 95% confidence limit crossed the line of zero difference when there was 25 to 30 ml of liquid in the pericardium, implying that when the pericardium contains less liquid there is less than 2.5% probability that the open-ended catheter will record a pressure as great as the $P_{c}$ calculated. Comparisons based on mean diastolic pressures gave results very similar to those obtained with use of end-diastolic pressures. Despite this underestimation by the open-ended catheter, figures 3, 4A, and 4B and table 1 show that $P_{b}$ was close to the calculated pressure, regardless of the amount of fluid in the pericardium.

We also investigated whether the restraining effect of the pericardium could be measured when it was perforated by several holes. Figure 5 shows a representative experiment. The perforation of the pericardium caused only a slight downward shift of the left ventricular diastolic pressure-diameter relationship. Complete opening of the pericardium, however, shifted the pressure-diameter relationship markedly downward, indicating that the pericardium had exerted a restraining effect even when it was perforated. As expected,

**TABLE 1**

<table>
<thead>
<tr>
<th>Absolute and relative differences between measured and calculated pericardial end-diastolic pressures at various pericardial fluid volumes</th>
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<tbody>
<tr>
<td><strong>Pericardial fluid</strong></td>
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<tr>
<td><strong>Absolute differences</strong></td>
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<tr>
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<td>Balloon</td>
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<tr>
<td><strong>Relative differences (% of $P_{b}$)</strong></td>
</tr>
<tr>
<td>Catheter</td>
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<td>Balloon</td>
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FIGURE 4A. Measured and calculated pericardial pressure at various pericardial fluid volumes. Note that the balloon (●) measures pressures that approximate the calculated values (○). The open-ended catheter (■), however, measures pressures substantially below the calculated value unless the pericardium contains a significant volume of fluid.

FIGURE 4B. Differences between measured and calculated pericardial pressures at various pericardial fluid volumes. Pressure deviation is measured minus PPcalc. For the open-ended catheter the pressure differences are fitted to a quadratic curve (y = 0.5210x - 0.0068x² - 10.70, r = .72). For the balloon the pressure differences are fitted to a line (y = 0.0219x - 0.61, r = .18). Shaded areas indicate the 95% confidence intervals of the lines. The open-ended catheter significantly underestimates pericardial pressure unless there is at least 30 ml liquid within the pericardium. The flat balloon, however, approximates the calculated pressure regardless of the volume of fluid in the pericardium.

FIGURE 5. Pressure-diameter loops from a single experiment showing the effect of perforating the pericardium. (Abbreviations and symbols are as in figure 3.) Note that even with holes in the pericardium transmural diastolic PgL calculated by subtracting pressure in the flat balloon approximates the directly measured transmural PgL (see legend to figure 4). After holes are made in the pericardium, however, the pressure in the open-ended catheter approaches zero and the calculated transmural pressure is markedly higher than that directly measured.

PPp approached zero when the pericardium was perforated. PPp, however, was still elevated and was similar to the calculated value (figure 6).

Table 2 and figure 7 compare measured pericardial pressures to the calculated values using the product of DA-P and DSFW to assess left ventricular size. PPp was not significantly different from PPcalc (14.5 ± 0.6 vs 16.5 ± 1.3 mm Hg, respectively), whereas PPp approximated zero (0.4 ± 3.7 mm Hg; p < .04).

FIGURE 6. Effect of making four to five small incisions in the pericardium on pericardial pressures. PPp approached zero and was significantly less than the calculated value (p < .002). PPp decreased moderately, but was not significantly different from the calculated value.
TABLE 2
Calculated and measured pericardial end-diastolic pressures (mm Hg) with the pericardium empty when using $D_{AP} \times D_{S-FW}$ to assess left ventricular size

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>$PP_{calc}$</th>
<th>$PP_b$</th>
<th>$PP_e$</th>
</tr>
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<tbody>
<tr>
<td>2</td>
<td>16.2</td>
<td>15.4</td>
<td>-6.7</td>
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<td>13.9</td>
<td>4.9</td>
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<tr>
<td>5</td>
<td>20.0</td>
<td>15.7</td>
<td>-5.1</td>
</tr>
<tr>
<td>6</td>
<td>14.0</td>
<td>13.1</td>
<td>8.4</td>
</tr>
<tr>
<td>Mean</td>
<td>16.5</td>
<td>14.5</td>
<td>0.4*</td>
</tr>
<tr>
<td>± SE</td>
<td>1.3</td>
<td>0.6</td>
<td>3.7</td>
</tr>
</tbody>
</table>

* $p < .04$ compared with $PP_{calc}$.

Discussion

To assess the accuracy of our methods for measuring pericardial constraint we assumed that static equilibrium conditions apply to the left ventricular free wall endocardial surface so that a calculated value of pericardial pressure could be obtained. This $PP_{calc}$ was used as a standard to evaluate the pericardial pressures measured directly by means of the open-ended catheter or the flat liquid-containing balloon. Our data show that unless the pericardium contains at least 30 ml of fluid, $PP_e$ substantially underestimates the restraining effect. The flat balloon, however, measures the pericardial restraining effect appropriately regardless of the amount of fluid in the pericardium.

A fundamental property of pressure as conventionally defined (i.e., "liquid pressure") is that it is exerted equally in all directions (Pascal's law). In contrast, in this situation "surface pressure" is equal to liquid pressure plus the contact stress exerted normally by one surface on the other.4 7 When the pericardium was empty, liquid pressure (the pressure measured with the open-ended catheter) was near zero (moments before this recording the pericardium had been connected to a suction of several millimeters of mercury). Under these same conditions the surface pressure (measured with the balloon) was approximately 13 mm Hg (the animals had been transfused so that left ventricular end-diastolic pressure was 20 ± 1.7 mm Hg). As fluid was infused into the pericardium liquid pressure increased rapidly (5 ml raised liquid pressure to approximately 8 mm Hg). Presumably the liquid pressure increased according to the well-known steep pressure-volume relationship of the pericardium.2 Probably the increase in pericardial volume was less than the volume infused since the heart may have become smaller during the infusion.9 As the liquid was infused the heart tended to be buoyed up and the contact stress diminished such that the epicardial surface pressure (the sum of the liquid pressure plus the contact stress) did not increase. Although in these experiments sufficient fluid was not infused to demonstrate the point clearly, when the pericardium contained large amounts of fluid surface pressure approximated liquid pressure. This implies that contact stress was zero, as might have been expected if the heart floated freely in a large pericardial effusion.

The experiment in which we perforated the pericardium when it contained 50 ml of liquid can be understood similarly. As noted, when the pericardium contained 50 ml of liquid, surface pressure was equal to liquid pressure, which was approximately 15 mm Hg. As the pericardium was incised the 15 mm Hg liquid pressure (exerted equally in all directions) forced the liquid out through the incisions. Liquid escaped until there was no liquid pressure gradient. However, the contact stresses exerted by the incised but otherwise intact pericardium were still considerable (approximately 10 mm Hg). Apparently, diastolic left ventricular filling can be restrained by a relatively unyielding netlike structure, even though the liquid pressure at the epicardial surface is zero.

Our experimental protocol might be criticized in that opening the pericardium could have changed the shape of the ventricle to an important degree. The effect could have been to invalidate our use of $PP_{calc}$ as a gold standard. To answer this possible criticism we used the product of the $D_{AP}$ and $D_{S-FW}$ as a volume

![FIGURE 7](http://circ.ahajournals.org/)

**FIGURE 7.** Left ventricular pressure ($PL_{LV}$) vs the product of $D_{AP}$ and $D_{S-FW}$ with the pericardium empty (dog No. 2). Transmural $PL_{LV}$ calculated by subtracting $PP_b$ (□) approximates the directly measured transmural pressure (i.e., $PL_{LV}$ with pericardium open [smaller symbols]). However, $PP_e$ is negative and transmural $PL_{LV}$ obtained by subtracting $PP_e$ (△) deviates considerably from the directly measured transmural pressure. ● = $PL_{LV}$ with pericardium closed.

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parameter and repeated the analysis in the four dogs in which these data were available (figure 7 and table 2). Since this analysis confirms the accuracy of the PP\textsubscript{d} value it is exceedingly unlikely that different stresses induced by shape changes at pericardectomy are important.

Kenner and Wood\textsuperscript{1} found no consistent increase in pericardial (liquid) pressure in closed-chest dogs when cardiac (fluoroscopic) size was increased by pulmonary arterial and aortic constrictions. As suggested by the present study the lack of increase in pericardial pressure might be related to the use of an open-ended catheter and inadequate volumes of liquid (<30 ml) in the pericardium. Interestingly, Kenner and Wood found that mean right atrial pressure, which is an excellent indicator of pericardial surface pressure when cardiac volume is changed by changing blood volume,\textsuperscript{2,10} was increased by 26 cm H\textsubscript{2}O during pulmonary arterial constriction. However, we do not know what the relationship between right atrial and pericardial surface pressure is during pulmonary arterial constriction. We predict that, for a given increase in right atrial pressure, pericardial surface pressure will increase less during pulmonary arterial constriction than when the increase in right atrial pressure is caused by intravenous infusion of fluid, which increases the volume of all chambers of the heart.

Holt et al.\textsuperscript{2} reported a model in which pericardial pressure measured by a flat balloon was somewhat higher than that measured by an open-ended catheter. However, since there is no further information about calibration of the balloons, it seems possible that their balloons were overfilled. Very recently Tyson et al.\textsuperscript{11} have reported results of an experimental study that support the approach of Kenner and Wood. (Except that catheter-tipped micromanometers are free of certain transmission artifacts the approaches are identical in that Tyson et al. measured hydrostatic pressure in the liquid near the heart.) The degree to which the data from this study are internally consistent leads us to conclude that sufficient fluid was present to make liquid pressure indistinguishable from surface pressure. This is only an assumption, however, since the authors do not clearly indicate how much fluid was present at the time of measurement (in the absence of pericardial effusion) and we cannot estimate from our experience how much fluid would be required in their surgically prepared dogs. Nonetheless, the results of Tyson et al. do not contradict our basic conclusion: flat balloons and open catheters or catheter-tipped manometers measure pressures that are fundamentally and qualitatively different and these differences may be physiologically important when the pericardium is empty or when it is unsealed.

We do not claim to have measured pericardial pressure absolutely physiologically. Pericardial volume probably was reduced to some degree when the pericardium was resealed. Different experimental designs\textsuperscript{12} should be used to define the magnitude of pericardial pressure under normal circumstances.

In conclusion, the present study demonstrates that the restraining effect of the pericardium can be measured with a flat liquid-containing balloon in the pericardial cavity. However, an open-ended liquid-filled catheter significantly underestimates the restraining effect unless the pericardium contains at least 30 ml of fluid. Furthermore, these data and those from our other study relating right atrial to pericardial pressure\textsuperscript{11} suggest that pericardial pressure represents an important fraction of left ventricular end-diastolic pressure even when the latter is very moderately elevated. This may imply an important role of the pericardium in the genesis of the elevated intracavitary pressures associated with (acute) cardiac failure.

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